

Harmful effect of immunotherapy in children with combined snail and mite allergy

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Background: With respect to allergy, the possibility of cross-reactivity between snail and mite is well recognized, and anecdotal reports suggesting that allergen immunotherapy with mite extract can worsen snail-induced allergy exist.

Objective: We describe the effect of immunotherapy in 4 children with snail-mite allergy.

Methods: Four children (1 boy and 3 girls; 9-13 years of age) had consistent clinical histories (mild immediate respiratory symptoms after ingestion) and positive skin reactions for allergy to snail. They also had mite-induced asthma and were therefore prescribed subcutaneous specific immunotherapy and subsequently followed.

Results: Several months (8-25) after starting immunotherapy, all children experienced life-threatening reactions, anaphylaxis, and respiratory failure after inadvertent ingestion of snail. Skin reactivity to the fresh food increased in all patients.

Conclusions: This observation confirms that in patients with combined mite-snail allergy, immunotherapy should be avoided. (J Allergy Clin Immunol 2002;109:627-9.)

Key words: Food allergy, snail, house dust mite, immunotherapy

Adverse reactions to food are of considerable importance in our society, but their diagnosis and management are often difficult. One of the most important aspects of adverse reactions to food is the cross-reactivity between proteins contained in different foods, or even between foods and aeroallergens. The cross-reactivity between vegetables and pollens and that between latex and vegetables are paradigmatic examples of this phenomenon. Lipid transfer proteins and profilins have been indicated as being responsible for these cross-reactions,¹ which lead, for instance, to the clinical presentation of oral allergy syndrome in patients with respiratory allergy.

Abbreviations used

IT: Immunotherapy

DBPCFC: Double-blinded, placebo-controlled food challenge

HDM: House dust mite

Allergy to snail is a very particular and interesting clinical model involving the cross-reactivity between 2 phylogenetically distant allergens: house dust mite (HDM) and snail. It is well known that patients with respiratory allergy due to HDM might have snail-induced food allergy and vice versa.²⁻⁴ Snail allergy can provoke respiratory symptoms (ie, asthma and rhinitis) as well as skin reactions (urticaria/angioedema) and anaphylaxis. Tropomyosin has been identified as one of the possible cross-reacting proteins.⁵

The immunologic role of immunotherapy (IT) in food-inhalant cross-reactions is unclear, because variable outcomes have been reported, depending on the allergen. We describe the harmful effect of IT with mite extract in 4 children with ascertained combined allergy to HDM and snail.

METHODS

Four children (1 boy and 3 girls) with snail-induced food allergy and mild asthma due to mites were studied. Their sensitization was well documented by means of skin prick tests and RAST assay. The panel of inhalatory allergens included mites, grasses, Parietaria, olive, birch, cat and dog dander, *Cladosporium*, and *Alternaria*, as well as negative (diluent) and positive (histamine) controls. A prick-by-prick test with fresh snail was also performed. The skin reactivity index was expressed as the mean of the major diameter of the wheal and its orthogonal; an index equal to or greater than 3 mm was considered positive. A RAST assay for snail was not available.

A double-blinded, placebo-controlled food challenge (DBPCFC) was carried out to better define the diagnosis. Each of the capsules of opaque gelatin (Lofarma S.p.A., Milan, Italy) contained 40 mg of dried snail or dextrose. The starting dose of 40 mg was increased every 30 minutes until objective symptoms appeared or until a cumulative dose of 8 g had been administered. The effect of DBPCFC was assessed by pulmonary function tests (Vitalograph Compact Spirometer, Buckingham, United Kingdom) every 20 minutes. A decrease of more than 20% from the baseline of FEV₁ was considered positive.

All children were prescribed subcutaneous specific IT (Abellò, Madrid, Spain) to dust mite to treat their respiratory allergy. The

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TABLE I. Demography and diagnostic procedures

Case no.	Age (y)	Sex	Duration of asthma (y)	Skin test: mite*	Prick-by-prick test: snail*	RAST HDM (KU/L)	DBPCFC
1	12	M	9	10 mm	9 mm	30.4	Asthma and rhinitis: decrease FEV ₁ 20% after 120 mg
2	13	F	8	8 mm	7 mm	6.2	Asthma: decrease FEV ₁ 20% after 400 mg
3	12	F	7	8 mm	10 mm	15	Negative
4	9	F	3	8 mm	4 mm	9.7	Negative

DBPCFC, Double-blinded, placebo-controlled food challenge; M, male; F, female.

*(Major diameter + orthogonal)/2.

TABLE II. Outcomes of immunotherapy

Case no.	Before IT		After IT	
	Snail allergy symptoms	Prick-by-prick test: snail*	Snail allergy symptoms (first episode after IT began)	Prick-by-prick test: snail*
1	Asthma, 3 episodes in 4 y	9 mm	Severe asthma, recall urticaria after 17 mo	12 mm
2	Asthma, 5 episodes in 8 y	7 mm	Anaphylaxis, recall urticaria, respiratory failure after 15 mo	14 mm
3	Asthma, edema of lips, 2 episodes in 3 y	10 mm	Asthma, laryngeal edema, respiratory failure after 8 mo	18 mm
4	Cough and rhinitis, 5 episodes in 3 y	4 mm	Asthma, laryngeal edema, respiratory failure after 25 mo	14 mm

*(Major diameter + orthogonal)/2.

extract was standardized after an in-house reference and contained *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* in equal proportions. After a build-up phase with increasing doses, the maximum tolerated dose was administered once a month. Subsequently, all subjects underwent monthly clinical visits.

RESULTS

The 4 patients had consistent clinical histories of bronchial asthma due solely to HDM. In fact, no positive skin reaction other than HDM was detected, and the RAST assay confirmed these results. Furthermore, the prick-by-prick test with fresh snail showed a clearly positive reaction. Two children had positive responses to the DBPCFC, as demonstrated by a 20% fall in FEV₁ after the first doses of the masked food, whereas the other 2 children did not react to the maximum dose administered. These results are summarized in Table I.

Before IT was begun, the ingestion of snail repeatedly provoked immediate (within 30 minutes) symptoms in all children. The episodes were mild or moderate; they were always treated at home, and no hospitalization or emergency care was ever required. After IT was begun, the first inadvertent ingestion of snail caused all patients to develop severe, life-threatening systemic reactions requiring emergency care assistance and even mechanical ventilation (Table II). Two children also showed recall urticaria at the site(s) of IT injection. A significantly increased positive result of the prick-by-prick test with fresh snail was invariably observed after IT was begun (Wilcoxon: $P = .01$), whereas the skin reaction and RAST to HDM remained unchanged. Because of the severity of the reactions, the Ethics Committee denied permission to repeat the DBPCFC.

DISCUSSION

In clinical practice it is well known that cross-reactions between foods and inhalatory allergens can occur. Cross-reactions are particularly frequent with tree pollens and fresh vegetables. A cross-reactivity between mite and snail is more rare, though it has been occasionally described.²⁻⁴

When both environmental and food allergens are responsible for clinical manifestations, allergen avoidance would be the best approach, whereas desensitizing therapy toward one of the allergens does not necessarily imply desensitization toward the other. This latter aspect has been only partly investigated in recent years, and few studies are available. In the case of oral allergy syndrome associated with vegetables, claims have been made that pollen IT can improve oral symptoms,^{6,7} though in a number of patients the food allergy symptoms worsened. In the case of allergy to HDM and snail, only 2 reports are presently available, both suggesting that IT might worsen food allergy.^{8,9} In the present study, we carefully followed 4 children with asthma due to mites and systemic manifestations of food allergy due to snails. Indeed, 2 of the children had a negative DBPCFC result, but positive skin test results and the reproducibility of symptoms confirmed the etiologic role of snails. One could hypothesize that the amount of allergen administered in the challenge was not high enough to elicit a reaction. In fact, the maximum dose of snail used in the DBPCFC was greatly inferior to that consumed in a normal meal. On the other hand, it is known that DBPCFCs can sometimes provide negative results,¹⁰ and it is recommended that negative blinded challenges must be followed by an open feeding. In our patients, an open feed-

ing under controlled conditions was not performed after the DBPCFC, but the clinical evidence (ie, worsening of symptoms after natural feeding) makes us confident that the result of an open challenge would have been positive.

In the 4 children studied, mite IT invariably worsened the clinical presentation of the food allergy; the new episodes of reaction to snail after IT was begun were all life-threatening. In addition, the positive prick-by-prick reaction to snail increased significantly in all patients.

On the basis of our results, we suggest that in the case of ascertained mite-snail combined allergy, specific IT to mite should be avoided because of the unfavorable risk/benefit ratio.

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